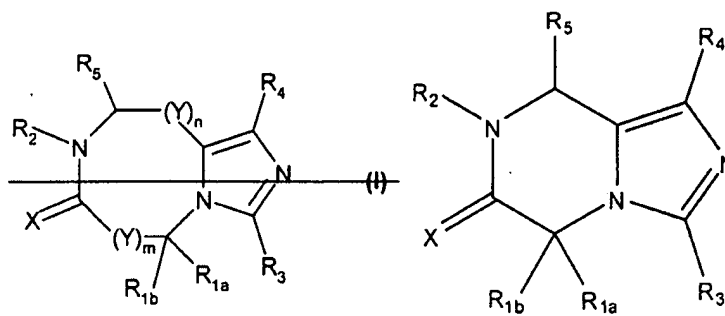


Claims 1-27 (cancelled)

Claim 28 (Currently Amended) A compound of the formula I



wherein

X is oxygen or H₂;

~~Y is -CRR' in which~~

~~R and R' are independently hydrogen, optionally substituted alkyl, aralkyl or heteroaralkyl;~~

~~R_{1a} is hydrogen, optionally substituted alkyl, cycloalkyl, alkenyl, alkynyl, monocyclic or bicyclic aryl or aryl, aralkyl, optionally substituted monocyclic or bicyclic heteroaryl heterocyclyl or heteroaralkyl provided that R_{1a} is not 9H-carbazol-2-yl or 9H-fluoren-2-yl when R₂ is methyl, m is zero or an integer of 1, n is zero, X is H₂ and R_{1b}, R₃, R₄ and R₅ are hydrogen;~~

~~R_{1b} is hydrogen, optionally substituted alkyl, or aralkyl, heteroaralkyl, aryl or heteroaryl provided that: R_{1a} and R_{1b} combined are alkylene which taken together with the carbon atom to which they are attached form a 3 to 6 membered ring;~~

~~R₂ is R₆-(CHR₇)_p in which~~

~~R₆ is optionally substituted alkyl, cycloalkyl, aryl or heterocyclyl;~~

~~R₇ is hydrogen, optionally substituted alkyl, aryl, heteroaryl or aralkyl;~~

~~p is zero or an integer from 1 to 4;~~

~~R₃ and R₄ are independently hydrogen, halogen, optionally substituted alkyl, aryl or heteroaryl; or~~

~~R₄-C may be replaced by nitrogen;~~

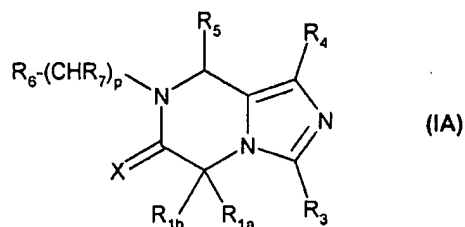
~~R₅ is hydrogen, optionally substituted alkyl, aryl, heteroaryl, aralkyl or heteroaralkyl;~~

~~m and n are each zero;~~

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 29-30 (Cancelled).

Claim 31 (Currently Amended) A compound according to claim 28 of formula IA



wherein

X is oxygen or H₂;

R_{1a} is ~~lower alkyl, aryl~~ monocyclic or bicyclic aryl or heteroaryl ~~provided that R_{1a} is not 9H-carbazol-2-yl or 9H-fluoren-2-yl when R₆ is methyl, p is zero, X is H₂, and R_{1b}, R₃, R₄ and R₅ are hydrogen;~~

R_{1b} is hydrogen, lower alkyl, or ~~aralkyl or heteroaralkyl~~;

R₆ is cycloalkyl, aryl or heteroaryl;

R₇ is hydrogen or lower alkyl;

p is zero or an integer of 1 or 2;

R₃, R₄ and R₅ are hydrogen;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

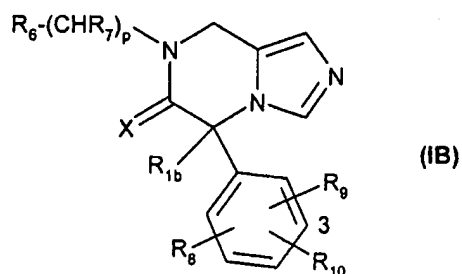
Claim 32 (Previously Presented) A compound according to claim 31 wherein

R_{1a} is monocyclic aryl;

R_{1b} is hydrogen, lower alkyl or aralkyl;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 33 (Previously Presented) A compound according to claim 32 of formula IB



wherein

X is oxygen or H₂;

R_{1b} is hydrogen, lower alkyl or aralkyl;

R₆ is cycloalkyl, aryl or heteroaryl;

R₇ is hydrogen or lower alkyl;

p is zero or an integer of 1 or 2;

R₈, R₉ and R₁₀ are independently hydrogen, hydroxy, halogen, cyano, nitro, trifluoromethyl, optionally substituted alkyl, cycloalkyl, optionally substituted amino, alkoxy, alkylthio, carboxy, sulfonyl, carbamoyl, aryl, aryloxy, arylthio or heterocyclyl;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 34 (Previously Presented) A compound according to claim 33 of wherein

X is oxygen or H₂;

R_{1b} is hydrogen, lower alkyl or aralkyl;

R₆ is cycloalkyl, aryl or heteroaryl;

R₇ is hydrogen or lower alkyl;

p is an integer of 1;

R₈ is hydrogen;

R₉ is hydrogen, halogen, cyano or trifluoromethyl;

R₁₀ is halogen, cyano or trifluoromethyl;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 35 (Previously Presented) A compound according to claim 34 wherein

X is oxygen;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 36 (Previously Presented) A compound according to claim 34 wherein

R₈ is C₃₋₆cycloalkyl, monocyclic aryl or monocyclic heteroaryl;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 37 (Previously Presented) A compound according to claim 34 wherein

R₁₀ is located at the 3-position;

or a pharmaceutically acceptable salt thereof; or a diastereomer thereof; or a mixture of diastereomers thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 38 (Previously Presented) A compound according to claim 28 which is selected from:

- 4-(7-Cyclopropylmethyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-(7-Methyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-(7-Benzyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-(7-Allyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-(6-Oxo-7-propyl-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-(7-Isopropyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
- 4-{7-[2-(4-Fluoro-phenyl)-ethyl]-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl}-benzonitrile;
- 4-[7-(3-Morpholin-4-yl-propyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 7-(4-Methoxy-benzyl)-5-(4-thiophen-3-yl-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
- 4-[7-(4-Methyl-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 4-[7-(4-Chloro-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 4-[6-Oxo-7-(4-trifluoromethyl-benzyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 4-[6-Oxo-7-(3-methyl-benzyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 4-[6-Oxo-7-(4-fluoro-benzyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
- 4-[6-Oxo-7-(3-trifluoromethyl-benzyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;

4-[6-Oxo-7-(3, 4-dichloro-benzyl)- 5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-(7-Cyclopropyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 4-(7-Cyclohexyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 4-(7-Cyclopentyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 4-[7-(2-Methoxyethyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-[7-(3-Methoxypropyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-(6-Oxo-7-pyridin-4-ylmethyl-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 7-Benzyl-5-phenyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Methyl-5-phenyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-methyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-methoxy-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-cyclopropylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Benzyl-5-(4-bromo-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-chloro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-trifluoromethyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-methoxy-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-fluoro-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-methyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-cyclohexyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-methoxy-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-cyclopropylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Benzyl-5-(3-bromo-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-methoxy-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-chloro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-methyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-trifluoromethyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(3-trifluoromethyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;

5-(3-Bromo-phenyl)-7-(3-fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(3-methyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-methoxy-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-chloro-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(3-chloro-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-methyl-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-(4-fluoro-phenethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-thiophen-2-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-furan-2-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-thiophen-3-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-furan-3-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-pyridin-3-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-pyridin-2-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-pyridin-4-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-cyclohexylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 4-[5-(3-Bromo-phenyl)-6-oxo-5,6-dihydro-8H-imidazo[1,5-a]pyrazin-7-ylmethyl]-piperidine-1-carboxylic acid *t*-butyl ester;
 5-(3-Bromo-phenyl)-7-piperidin-4-ylmethyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*R*)-5-(3-Bromo-phenyl)-7-((*R*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*S*)-5-(3-Bromo-phenyl)-7-((*R*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*R*)-5-(3-Bromo-phenyl)-7-((*S*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*S*)-5-(3-Bromo-phenyl)-7-((*S*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*R*)-5-(4-Bromo-phenyl)-7-((*R*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*S*)-5-(4-Bromo-phenyl)-7-((*R*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*R*)-5-(4-Bromo-phenyl)-7-((*S*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 (*S*)-5-(4-Bromo-phenyl)-7-((*S*)-1-phenyl-ethyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 4-[(*R*)-6-Oxo-7-((*S*)-1-phenyl-ethyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-[(*S*)-6-Oxo-7-((*S*)-1-phenyl-ethyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;

7-Benzyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-(4-Methyl-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-(4-Fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 3-(7-Benzyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 3-[7-(4-Methyl-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 3-[7-(4-Fluoro-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 3-[7-(4-Chloro-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 3-[7-(4-Methoxy-benzyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 3-[7-(4-Fluoro-phenethyl)-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 3-(7-Phenethyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 3-(7-Cyclopropylmethyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 5-(4'-Chloro-biphenyl-4-yl)-7-(4-methoxy-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-(4-Methoxy-benzyl)-5-(4-thiophen-3-yl-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Cyclopropylmethyl-5-(4-thiophen-3-yl-phenyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Benzyl-5-(4'-fluoro-biphenyl-3-yl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-Biphenyl-4-yl-7-(4-fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 7-Benzyl-5-biphenyl-3-yl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 Methyl 4-(7-benzyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzoate;
 4-(7-Benzyl-5-methyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;
 5-(4-Bromo-phenyl)-7-cyclopropylmethyl-5-methyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(3-Bromo-phenyl)-7-cyclopropylmethyl-5-methyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 5-(4-Bromo-phenyl)-7-(4-fluoro-benzyl)-5-methyl-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;
 4-[7-(4-Fluoro-benzyl)-5-methyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-[(R)-7-[(S)-1-(4-Fluoro-phenyl)-ethyl]-5-methyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 4-[(S)-7-[(S)-1-(4-Fluoro-phenyl)-ethyl]-5-methyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl]-benzonitrile;
 5-Benzyl-5-(4-bromo-phenyl)-7-(4-fluoro-benzyl)-7,8-dihydro-imidazo[1,5-a]pyrazin-6-one;

4-(5,7-Dibenzyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile;

4-(5-Benzyl-7-cyclopropylmethyl-6-oxo-5,6,7,8-tetrahydro-imidazo[1,5-a]pyrazin-5-yl)-benzonitrile; and

5-(4-Bromophenyl)-7-(4-methoxy-benzyl)-5,6,7,8-tetrahydro-imidazo[1,5-a]-pyrazine;

or a pharmaceutically acceptable salt thereof; or an optical isomer thereof; or a mixture of optical isomers thereof.

Claim 39 (Previously Presented) A method for the inhibition of aldosterone synthase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 40 (Previously Presented) A method for the prevention and/or treatment of conditions associated with aldosterone synthase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 41 (Previously Presented) The method according to claim 40, which method comprises administering said compound in combination with a therapeutically effective amount of anti-obesity agent, anti-hypertensive agent, inotropic agent or hypolipidemic agent.

Claim 42 (Previously Presented) A method for the treatment of hypokalemia, hypertension, congestive heart failure, atherosclerosis, coronary heart diseases and post myocardial infarction, which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 43 (Previously Presented) A method for the treatment of restenosis, increased formation of collagen, fibrosis, and remodeling following hypertension and endothelial dysfunction, which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 44 (Previously Presented) A method for the treatment of renal failure and nephropathy, which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 45 (Previously Presented) A method for the treatment of syndrome X and obesity, which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of claim 28.

Claim 46 (Currently Amended) A pharmaceutical composition comprising ~~a therapeutically effective amount of~~ a compound of claim 28 in combination with one or more pharmaceutically acceptable carriers.

Claim 47 (Previously Presented) A pharmaceutical composition according to claim 46 for the treatment of hypokalemia, hypertension, congestive heart failure, atherosclerosis, coronary heart diseases, post myocardial infarction, restenosis, increased formation of collagen, fibrosis, remodeling following hypertension and endothelial dysfunction, renal failure, nephropathy, syndrome X and obesity.

Claim 48 (Currently Amended) A pharmaceutical composition comprising ~~a therapeutically effective amount of~~ a compound of claim 28 in combination with a therapeutically effective amount of anti-obesity agent, anti-hypertensive agent, inotropic agent or hypolipidemic agent.

Claim 49 (Previously Presented) A pharmaceutical composition according to claim 48 for the treatment of hypokalemia, hypertension, congestive heart failure, atherosclerosis, coronary heart diseases, post myocardial infarction, restenosis, increased formation of collagen, fibrosis, remodeling following hypertension and endothelial dysfunction, renal failure, nephropathy, syndrome X and obesity.